REMARKS

Claims 43-50 and 56-58 are pending in the application. Claims 43-58 were examined and rejected.

Claims 51-55 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claims 43-45 and 50 are amended. The amendments were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection. No new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claims 43-59 are rejected for failing to meet the enablement requirement of 35 U.S.C. §112, first paragraph.

In making this rejection, the Office generally asserts that the data set forth in the instant specification are insufficient to support the claims, and, accordingly, the specification fails to enable the claims. In particular, the Office asserts that the specification fails to provide sufficient data specifically relating to SEQ ID NO:3. The Applicants respectfully traverse this rejection.

The Applicants respectfully submit that "SEQ ID NO:3", "SK2", "CHIR-8", "Candidate ID 181" and "CLUSTER 9083" refer to the same gene: a gene that encodes the nucleotide sequence of SEQ ID NO:3. As described in the application, clustering is used to group clones so that the polynucleotides assigned to the same cluster overlap in sequence (see paragraph [00219]). In other words, "SEQ ID NO:3" and "CLUSTER 9083" are both names for the same polynucleotide. This is indicated in table 2 on page 76 of the instant specification..

For the Examiner's convenience, the relevant fields of Table 2 are set forth below:

Table 2. Polynucleotide sequence identification and characterization

SEQ ID NO	CLUSTER	Candidate ID	CHIR	SEQ NAME	ORF start	ORF stop	SEQ ID NO of encoded polypeptide
3	9083	181	CHIR-8	SK2	219	693	4

Accordingly, when data pertaining to "CLUSTER 9083" are provided, the data also pertain to SEQ ID NO:3,. "SEQ ID NO:3" was selected for use in the claims because it refers to a sequence set forth in the Sequence Listing of the application, which sequence is representative of the gene identified by the cluster.

Table 3 of the instant application shows that polynucleotides corresponding to SEQ ID NO:3 (also known as cluster 9083) are found in cDNA libraries made from primary and metastasized colon tumors, but not normal colon, from a single patient (patient #2). Accordingly, the data set forth in Table 3 indicate that expression of a gene identified by SEQ ID NO:3 is induced in cancerous cells.

For the Examiner's convenience, the relevant fields of Table 3 are set forth below:

Table 3							
SEQ ID NO	CLUSTER	Normal (Lib15) Clones	Tumor (Lib16) Clones	High Met (Lib17) Clones	Tumor/Normal (Lib16/Lib15)	High Met/Normal (Lib17/Lib15)	High Met/Tumor (Lib17/Lib16)
3	9083	0	10	14	10	14	1

Lib 15, Lib 16, and Lib 17 are described in the specification as follows (table following paragraph [00216]). The relevant portion of this disclosure is provided below for the Examiner's convenience:

Table 1. Description of cDNA Libraries

Library	Description	Number of Clones
15	Normal Colon - UC#2 Patient (MICRODISSECTED PCR (OligodT) cDNA library)	282718
16	Colon Tumor - UC#2 Patient (MICRODISSECTED PCR (OligodT) cDNA library)	298829
17	Liver Metastasis from Colon Tumor of UC#2 Patient (MICRODISSECTED PCR (OligodT) cDNA library)	303462

The results set forth in Table 3 alone, and in view of the sources of the libraries as summarized in Table 1, are adequate to show that expression of the gene identified by SEQ ID NO:3 is induced in cancerous cells, and, accordingly, that the gene may be used as a marker for colon cancer.

In order to show that expression of the gene identified by SEQ ID NO:3 is induced in colon cancers of more than one patient, the Applicants investigated cancers from a total of four patients, this time using PCR primers that are specific for SEQ ID NO:3 (a.k.a. cluster #9083). This data is presented in the table shown below. The table shows that expression of the gene identified by SEQ ID NO:3 is significantly upregulated in three of the four patients tested (i.e., 75% of the patients).

For the Examiner's convenience, this table is reproduced below. As discussed in the specification, "N", "PT" and "MET" refer to normal tissue, primary tumor and metastasized tumor, respectively.

Cluster#9083 (SK2): overexpression in 3 of 4 patients (75%)			
Patients	N	PT	MET
UC#1	0.0021	0.0013	0.0078
UC#2	0.008	0.012	0.014
UC#4	0.0021	0.0022	0.0026
UC#7	0.0009	0.0021	0.0039

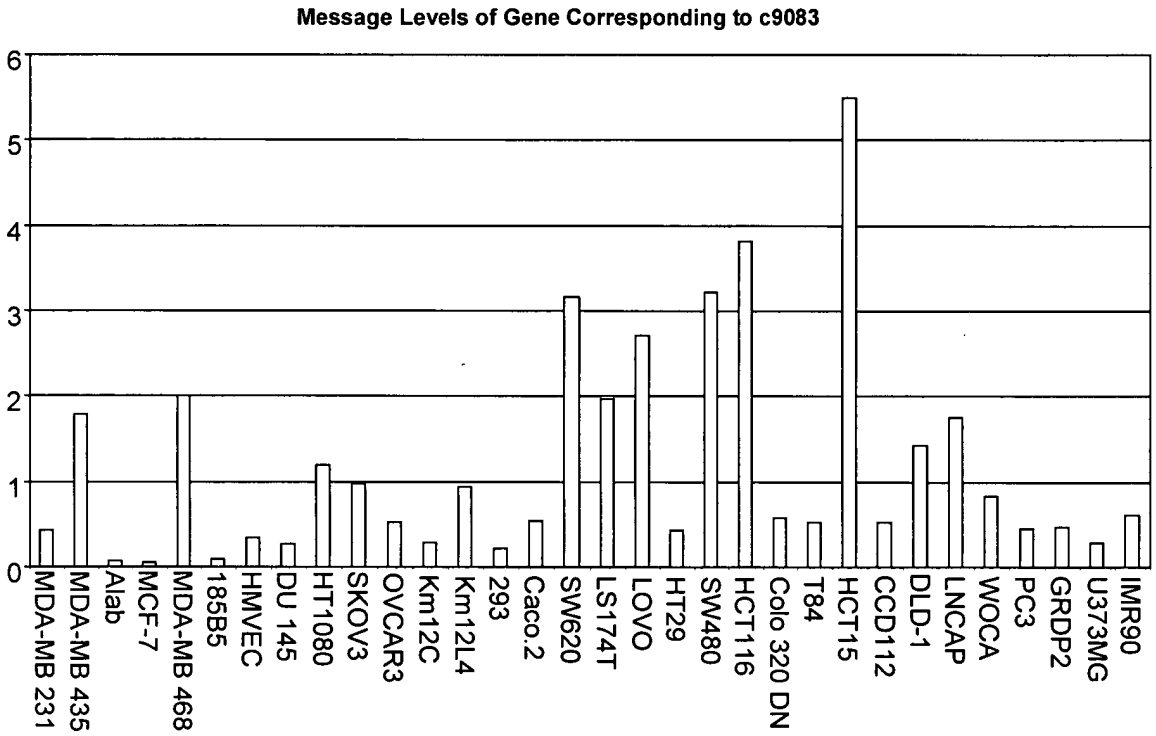
The results set forth in this table are adequate to show that expression of the gene identified by SEQ ID NO:3 is induced in cancerous cells of several different patients. Like almost every other diagnostic test, this test does not identify a cancerous cell 100% of the time. However, the claims do not require this to be the case. For example, the claims do not state that if the gene identified by SEQ ID NO:3 is *not* differentially expressed, then the cell is not cancerous. Rather, the claims only recite that if the gene identified by SEQ ID NO:3 *is* differentially expressed relative to a control level, such is indicative that the cell is cancerous.

More to the point -- satisfaction of the requirements of 35 U.S.C. §112, ¶1 do not require such. In view of the data set forth in this table, the Applicants respectfully submit that one of skill in the art would recognize that expression of the gene identified by SEQ ID NO:3 is significantly upregulated in many, if not most or all, colon cancers.

Finally, the Applicants investigated the expression of the gene identified by SEQ ID NO:3 in various cell lines, including cancer cell lines from lung (IMR90), glioblastoma (I373MG), prostate (GRDP2, PC3, WOCA and LNCAP), colon (HCT15, HCT116, SW480, LOVO, and others), ovary (OVCAR3, SKOV3), sarcoma (HT1080), and breast (e.g., MDA-MB-468, MDA-MB-435, and MDA-MD-231). The data obtained from this investigation are shown in Fig. 1. The Applicants respectfully submit that these data show that expression of the gene identified by SEQ ID NO:3 is significantly upregulated in cancerous cells from a number of different tissues. It would therefore be reasonable to expect expression of the gene identified by SEQ ID NO:3 to be upregulated in many, if not most or all, types of cancer.

For the Examiner's convenience, Fig. 1 is reproduced below.

FIG. 1



Accordingly, in view of all of the data presented in the instant specification, the Applicants respectfully submit that one of skill in the art would recognize that there is a reasonable correlation between the expression of the gene identified by SEQ ID NO:3, and cancerous cells. Since a "reasonable

correlation" is all that is needed to meet the enablement requirement of 35 U.S.C. § 112[1], the Applicants respectfully submit that the instant application meets the enablement requirement of 35 U.S.C. § 112, first paragraph, and, accordingly, this rejection may be withdrawn.

The Office Action sets forth a position that is opposite to that of the Applicants. However, in view of the data set forth in the instant application, the Applicants respectfully submit that the Office's position is not fairly based. A number of assertions made by the Office are specifically addressed below.

One basis for the Office's position is a belief that the specification does not correlate the level of SEQ ID NO:3 expression with cancerous cells. However, as discussed above, the specification provides an overwhelming amount of data that shows that expression of a gene identified by SEQ ID NO:3 is induced in cancerous cells, as compared to normal cells, both *in vitro* and *in vivo*. Accordingly, the Applicants respectfully submit that one of skill in the art would recognize that the specification *does* correlate the level of expression of a gene identified by SEQ ID NO:3 with cancerous cells, in contrast to the Office's belief.

Another basis for the Office's position is a belief that data was only obtained from a single patient. However, as discussed above, data was obtained from *four* patients as well as over *30 different* cell lines. Accordingly, the Applicants respectfully submit that one of skill in the art would recognize that the specification provides data from more than one patient, in contrast to the Office's belief.

A further basis for the Office's position is a belief that the instant data was obtained from a sample of inadequate size, citing an Falzarano (Hawaii Med. J., 2003) and an NCI article on cancer prevention (found at http://www.cancer.gov/cancerinfo/pdq/prevention/overview). Falzarano, however, was a study designed to measure the efficacy of nurse endoscopists in colorectal screening in Hawaii. The NCI article described a study of cancer *prevention*, not detection. The Applicants respectfully submit that these references are not relevant to the claimed invention, which relates to cancer cell detection (*not* prevention) by detecting expression of a particular gene (*not* by endoscopy).

A final basis for the Office's position is an assertion that genetic alterations which occur in cells lines are not necessarily reflective of the genetic changes which occur *in vivo*. In support of this assertion, the Office cites Dermer et al (BioTechnology 1994 12:320). However, the Applicants

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[1] See MPEP § 2164.08 "Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims." Citing In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

respectfully submit that they have provided "*in vivo*" data (i.e. data showing that a gene identified by SEQ ID NO:3 is overexpressed in cancers of three human patients). In view of this data, in contrast to the Office's belief, one of skill in the art would recognize that expression of the gene identified by SEQ ID NO:3 *is* induced in cancer cells *in vitro* and *in vivo*. According to the guidance set forth in §2164.02[2], this data should be considered as showing working examples of the claimed invention.

In view of the foregoing, the Applicants respectfully submit that one of skill in the art, upon viewing the data presented in the instant specification, would reasonably conclude that expression of the gene identified by SEQ ID NO:3 is induced in cancerous cells, *in vitro* and *in vivo*. In order to practice the invention, all that one of skill in the art would have to do is determine whether that gene is induced in a test sample, as compared to a suitable control. Since gene expression assays (e.g., Northern blotting, RT-PCR) are well known in the art and described in great detail in the instant specification, the Applicants respectfully submit that one of skill in the art would be able to practice the claimed invention without undue experimentation. This is all that is required to meet the enablement requirement of 35 U.S.C. §112, first paragraph.

The Applicants respectfully submit that this rejection has been adequately addressed. Accordingly, this rejection may be withdrawn without further discussion.

Rejection under 35 U.S.C. §112, first paragraph (written description)

Claims 51-55 are rejected for failing to meet the written description requirement of 35 U.S.C. §112, first paragraph.

Without wishing to acquiesce to this rejection and solely to expedite prosecution, claims 51-55 are cancelled.

Accordingly, this rejection is moot and may be withdrawn.

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[2] The MPEP states at §2164.02: "An in vitro or in vivo animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention..... Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an in vitro or in vivo animal model example. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985)."

SUMMARY

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number 2300-1663.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: February 4, 2004

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